

(95%CI 1.44, 48.35) for patients with the VKORC1 TT (rs9923231) genotype compared with other genotypes. The mean cost of health care attributable to warfarin therapy was ≤ 392 . The management of warfarin-related adverse events contributed to 53% of the overall cost. The mean costs for those who experienced an adverse event was ≤ 884 (95%CI, 554, 1837) compared with ≤ 178 (95%CI, 164, 192) for the 179 patients who did not. **CONCLUSIONS:** Our analysis is the first to demonstrate a significant association between VKORC1 variant genotype and hospitalization. Although no independent effect on total cost was evident, carriers of VKORC1 TT were eight times more likely to be hospitalized due to adverse events.

PM3

USE OF PHARMACOGENETIC TESTING TO DETERMINE ADJUVANT HORMONAL THERAPY CHOICE IN EARLY STAGE BREAST CANCER PATIENTS: A VALUE OF INFORMATION ANALYSIS

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OBJECTIVES: To estimate the uncertainty regarding adjuvant treatment selection for postmenopausal women with early stage oestrogen-receptor positive breast cancer when pre-treatment CYP2D6 pharmacogenetic testing is considered as an option. In addition, the expected value of partial perfect information (EVPI) was estimated for different parameter sets to inform research prioritisation. **METHODS:** A decision analytic model estimated lifetime costs and quality adjusted life years (QALYs) for four comparators: 5 years of tamoxifen; 5 years of an aromatase inhibitor (AI); CYP2D6 test and treat wt/wt genotypes with tamoxifen and other genotypes with an AI; CYP2D6 test and treat wt/wt and wt/*4 genotypes with tamoxifen and *4/*4 genotypes with an AI. No trial data for CYP2D6 contingent treatment pathways were identified. Trial data comparing tamoxifen to anastrozole was therefore synthesised with observational data linking CYP2D6 genotype to recurrence in patients receiving tamoxifen. Estimates of the EVPI were derived by attaching distributions to input parameters and using two-level Monte Carlo simulation. EVPI estimates were generated for parameters describing the efficacy of tamoxifen and anastrozole; parameters describing genotype-specific tamoxifen efficacy; genotype prevalence; utility weights and health state costs. **RESULTS:** The strategy of CYP2D6 test and treat wt/wt patients with tamoxifen and all others with an AI maximised expected net benefit assuming a decision threshold of $\leq 30,000$ /QALY, and had an incremental cost-effectiveness ratio of $\leq 14,133$ /QALY. However, this maximised net benefit with only 61% certainty. This substantial decision uncertainty led to an expected value of perfect information estimate of ≤ 84 million. The EVPI estimate for parameters describing genotype-specific tamoxifen efficacy was ≤ 57 million. Estimates for other parameter groups were low. **CONCLUSIONS:** Further CYP2D6 genotyping studies amongst patients receiving tamoxifen should be prioritised. Expected value of sample information analysis could be used to establish the cost-effectiveness and optimal design of this primary research.

PM4

AN EXPLORATION OF THE POTENTIAL CLINICAL BENEFITS AND RISKS OF CYP2D6 TESTING TO GUIDE TAMOXIFEN THERAPY IN BREAST CANCER

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OBJECTIVES: Recent studies have reported that women receiving adjuvant tamoxifen with CYP2D6 poor metabolizer genotype have a higher risk of breast cancer recurrence than women without poor metabolizer genotype. The objective of this study was to evaluate pharmacogenetic testing for CYP2D6 variants as an approach to help clinicians identify postmenopausal women that would be better candidates for alternative therapies. **METHODS:** We developed a decision-analytic lifetime Markov model consisting of 6 health states and assessed a hypothetical cohort of 64-year old women with ER+ breast cancer receiving tamoxifen. We assumed women who were poor metabolizers would be switched to anastrozole. The incidence of local regional relapse, metastasis, and breast cancer death were obtained from the 2005 ATAC trial. The hazard ratio for disease recurrence in poor vs. extensive metabolizers was derived from a recent study by Goetz et al. Cost, utilities and background mortality rates were obtained from the published literature or publicly available sources. One-way sensitivity analyses and scenario analyses were conducted to evaluate uncertainty. **RESULTS:** Projected disease free survival at 5 years was 81.4% for tamoxifen and 83.3% for anastrozole, compared to 81.0% and 83.8% in the ATAC trial. Treatment with tamoxifen resulted in 11.95 QALYs, anastrozole 12.15 QALYs, and CYP2D6-guided treatment 12.19 QALYs. The testing strategy resulted in the greatest QALYs with a hazard ratio for recurrence in CYP2D6 variant versus wild-type patients of 1.66 or higher, or variant prevalence greater than 20%. **CONCLUSIONS:** Genetic testing for CYP2D6 status in postmenopausal women taking adjuvant tamoxifen may lead to clinically meaningful improvements in survival and quality of life. Evaluation of the relative impact of drug-related adverse events, validation of association studies, and assessment in ethnically diverse populations are needed before widespread testing can be recommended.

PODIUM SESSION I: RESEARCH ON METHODS – Utility Methods

UTI

ON THE ISSUE OF UTILITY MULTIPLICATION: A REVISIT

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OBJECTIVE: Several estimators exist when average utility scores are not available for patient populations with multiple disease conditions. The multiplicative estimator is a widespread choice among them. This study is to empirically test the accuracy of the multiplicative estimator and compare it with other estimators. **METHODS:** Using the pooled Medical Expenditure Panel Survey (MEPS) 2001 and 2003 data, a sample of 40,846 adults with EQ-5D preference-based index scores were categorized into 238 disease condition categories. Due to the MEPS sampling property, co-morbid pair categories with less than 100 individuals were excluded, which left us with 760 co-morbid pairs in total. The study focus was the bias from the estimators to the observed mean scores for each co-morbid pair, with the observed scores presumed to be the true value. The analyses were conducted using both the raw estimators and the rescaled (purified) estimators. Regressions and concordance correlation coefficients were also used to evaluate the agreement between the estimators and the observed scores. **RESULTS:** Using the rescaled approach, the scores estimated by multiplying the 2 mean scores of the corresponding disease conditions on average had a statistically significantly larger bias ($p < 0.0001$) from the observed ones (-0.043) than simply picking the smaller mean of the 2 paired conditions (minimum estimator, bias = 0.027). However, the multiplicative estimator had less bias than other estimators including the additive estimator (bias = -0.054), the larger mean (bias = 0.077), the average of the means (bias = 0.052), mean of the condition with smaller sample (bias = 0.053). Results produced by other analyses, including using the raw scores, all favored the minimum estimator than the multiplicative estimator. **CONCLUSIONS:** Multiplication is not a good estimate when the average utility score for patients with 2 disease conditions is not readily available. The lower of the 2 utility scores had the least error among those estimators that we compared.

UT2

ELICITING TIME TRADE-OFF AMOUNTS FOR HEALTH STATES IN HYPOTHETICAL INDIVIDUALS OF DIFFERENT AGES USING A DISCRETE CHOICE EXPERIMENT

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OBJECTIVE: To measure whether public values for health vary with the age of the affected individual. **METHODS:** We fielded a discrete choice experiment via the internet in December 2007 to measure preferences for different attributes of influenza-related health states: length of episode (days of illness), severity of illness (workdays lost), age of hypothetical affected individual (range: 1–85 yrs), and time-tradeoff amounts (1 day – 2 yrs). We also collected data on socio-demographic characteristics and experience with influenza illness. Respondents were 18 years and older and matched to reflect characteristics of the general US adult population ($n = 1012$). Response rate was 67%. Respondents were presented with pairs of illness profiles for a hypothetical individual and indicated the profile they preferred. Each respondent answered 8 discrete choice questions. A full factorial design was used. Discrete choice analysis using generalized estimating equations was used to evaluate the relative value of different attributes in the illness profile while controlling for socio-demographic characteristics and influenza experience. **RESULTS:** As measured by time-tradeoff amounts, respondents preferred shorter influenza episodes (total length) but did not significantly prefer fewer workdays lost if episode length was held constant. Respondents preferred to avert uncomplicated illness in very young children (1 year old child: odds ratio = 2.35, $p < 0.05$; 3 year old child: odds ratio = 3.21, $p < 0.01$) and older adults (85 year old: odds ratio = 2.41, $p < 0.05$) compared to a 35 year old adult. For an influenza-related hospitalization, respondents preferred to avert illness in very young children (1 year old child: odds ratio = 2.86, $p < 0.01$) compared to a 35 year old adult. **CONCLUSIONS:** Approaches that assume values for illnesses do not vary with the age of a patient may bias economic analyses that use these values. If patient age is likely to affect valuations, then age should be included as an attribute in the valuation exercise.

UT3

THE VALUE OF ADDED LIFE YEARS AS A FUNCTION OF AGE, PROGNOSIS AND QUALITY OF LIFE

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OBJECTIVE: Do people weigh gains in life years differently when patients differ in age (but not in life expectancy), life expectancy (but not in age) or QOL (but not age or life expectancy)? **METHODS:** Trade off questions were developed searching for indifference between giving healthy life years to patients with different ages, prognoses and quality of life. Data come from 46 heart failure patients, 60 healthy controls and 180 students. For age, as well as prognosis and QOL, six comparative sets were developed. Each respondent answered two questions of each set and two combination-questions. Ordered logistic regression was used in combination with conditional linear regression for “extreme” answers. Answers are “extreme” when, for example, one extra life year in a young patient is preferred to 10 in an old patient or when respondents can’t choose. **RESULTS:** More than 40% of the answers are “extreme”.